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CELLULAR MECHANISMS OF CENTRAL NERVOUS MODULATION(U)  
CAMBRIDGE UNIV (ENGLAND) DEPT OF ZOOLOGY J E TREHERNE  
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CELLULAR MECHANISMS OF CENTRAL NERVOUS MODULATION

BY Dr. J.E. Treherne

Department of Zoology, University of Cambridge, U.K.

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## Scientific Activities

A critical factor in our analysis of the mechanism of ionic homeostasis of the brain microenvironment, and its modulation by neurotransmitters, is the precise localization of the insect blood-brain barrier system.

This system limits the movements of water-soluble ions and small molecules between the blood and the neuronal surfaces, as has been demonstrated in electrophysiological experiments. It has been supposed to be located in the perineurium since extracellular tracers (peroxidase, microperoxidase and ionic lanthanum) permeate the neural lamella, but are unable to penetrate beneath the superficial layer of neuroglia. The tracers are capable of only limited entry into the clefts between the perineurial cells, which is suggested to be due to the intercellular junctional complexes, notably tight junctions.

The ultrastructural studies do not necessarily indicate an impermeability to smaller substances. It is known, for example, that brief exposure of cockroach connectives to hypertonic urea increases access of sodium, potassium and lithium ions to the axon surfaces but does not facilitate penetration of ionic lanthanum or microperoxidase.

A superficial diffusion barrier, at the perineurial level, is also difficult to reconcile with the rapid fluxes of radiocations which have been observed between the plasma and the central nervous tissues.

We have, however, recently provided further evidence that the blood-brain barrier is located in the perineurium, by recording with microelectrodes from perineurial cells, identified by injection of peroxidase.

The cockroach blood-brain barrier may be characterized electrophysiologically by recording the diffusion potentials that are generated across the barrier when the ionic composition of the external saline is altered. These potentials have been measured within giant axons, in the extracellular spaces immediately outside them, and with sucrose-gap recordings. We have now shown that these potential changes are at their largest amplitude within the perineurial cells, and only slightly attenuated immediately below this neuroglial layer. These observations

show that the potentials are generated across the outermost membranes of the perineurial cells, and the junctions joining the cells, and that this interface may therefore be identified as the blood-brain barrier for monovalent cations.

The information that we have now acquired indicates that the ionic composition of the immediate fluid environment of insect nerve cells appears to be achieved by a combination of passive and active processes involving the neuroglia and an extracellular anion matrix (see previous report). The peripheral intercellular diffusion barrier predicts the underlying extracellular system from fluctuations in the ionic composition of the blood plasma and from water-soluble toxic materials. However, it renders the neurones more susceptible to fluctuations in the chemical composition of their immediate, very restricted, fluid environment resulting from their electrical and metabolic activities. The passive role of the superficial neuroglial barrier is thus reinforced by glial and axonal cation pumping which, we postulate, tend to recycle sodium ions so as to maintain extracellular concentrations of this cation, at the same time, reduce the concentrations of released potassium ions during neuronal excitation. This effect could be augmented by a sodium reservoir associated with an extracellular anion matrix.

The above findings have laid a foundation to elucidate the value of octopamine in modulating these homeostatic mechanisms and especially the permeability of the blood-brain interface.

#### Publications

Treherne, J.E. & Schofield, P.K. (1981) Mechanism of ionic homeostasis

in the central nervous system of an insect. J. exp. Biol., 95, 61-73.

Treherne, J.E., Schofield, P.K. & Lane, N.J. (1982) Physiological and ultra-

structural evidence for an extracellular anion matrix in the central nervous system of an insect (Periplaneta americana). Brain Research (in the press).

Treherne, J.E. (1982). Maintenance: State of the Art Report (contributor).

In: Neuronal-glial Cell Interrelationships, pp.169-202 (Ed. T.A. Sears)

Springer-Verlag.

#### Future Research Plans

It is proposed to test the effects of octopamine and neurotransmitters on the electrical responses of identified perineurial cells. Measurements will also be made on the octopamine levels in the blood, in normal and stressed insects, and in central nervous tissues.

Preliminary observations will also be carried out on neuroglia in degenerating and regenerating central nervous connectives. This will involve in vivo observations and in vitro studies using organ culture techniques. It is hoped that this approach will induce massive glial proliferation. This should facilitate electrophysiological and ultrastructural studies on the glial elements and, in addition, could provide convenient preparations for the study of the chemical control of glial growth.

#### Significant administrative action

Dr. Colin Leech was appointed to replace Dr. Julian Dow on 1st September 1981. Mr. A. Davenport was appointed to a temporary Assistantship in Research from 1st October 1981 until 31 January 1982.

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